Articles

Community-Acquired Pneumonia in Adults

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Although the frequency of community-acquired pneumonia caused by *Streptococcus pneumoniae* continues to be high, studies show that *Mycoplasma pneumoniae, Chlamydia pneumoniae,* or *Legionella pneumophila* are the etiologic agents in 20% to 40% of community-acquired pneumonia in adults. The clinical presentation of pneumonia caused by these organisms may be indistinguishable from pneumonia due to *S pneumoniae.* Separation of cases of pneumonia due to *S pneumoniae* as typical and that caused by *M pneumoniae, C pneumoniae,* or *L pneumophila* as atypical is unwarranted and unhelpful in planning therapy. As many as 35% to 50% of patients do not have an etiologic agent identified. Community-acquired pneumonia can have high morbidity and mortality in patients who are older, have underlying lung disease, diabetes mellitus, or other comorbid conditions, or who have decreased immune function regardless of the specific etiologic agent. In choosing appropriate empiric antimicrobial therapy in hosts who are not immunocompromised, erythromycin and other macrolide antibiotics have the advantage of being effective against a wide range of pathogens likely to be encountered, including *S pneumoniae, M pneumoniae,* and *L pneumophila,* and of having some benefit against *C pneumoniae.* In other patients, the selection of antibiotic therapy can be based on age, clinical suspicion, epidemiologic data, and laboratory test results. Antimicrobial therapy can be directed at specific organisms when and if they are identified.

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Pneumonia continues to be a common respiratory tract disease affecting all age groups.[1-3] Despite the recent emphasis on the increasing frequency of tuberculosis, the importance of pneumonia in immunocompromised patients, and the high morbidity and mortality of hospital-acquired nosocomial pneumonia, community-acquired pneumonia remains an important problem both in patients who are otherwise healthy and in those who have underlying long-term respiratory or other diseases. The presence of newly described pathogens, a better understanding of the clinical presentation of pneumonia, new diagnostic methods, and changes in treatment recommendations make community-acquired pneumonia a continually evolving topic.[1-3] In particular, it is now apparent that clinical presentations of pneumonia due to *Streptococcus pneumoniae* and pneumonias caused by *Mycoplasma pneumoniae, Chlamydia pneumoniae, Legionella pneumophila,* viruses, or other agents cannot always be distinguished.[1] This finding casts doubt on a physician's ability to separate "typical" pneumonia from "atypical" pneumonia and thereby reliably use clinical features to guide the choice of diagnostic tests and initial therapy.

Pathogens and Epidemiology of Community-Acquired Pneumonia

In retrospective reviews, the precise agent responsible for pneumonia is unknown or uncertain in as many as 50% of patients, even with appropriate diagnostic studies.[1,4,5] Because treatment is often started and continued without knowledge of the actual pathogen, an epidemiologic approach may be helpful.

It is generally accepted that the cause of community-acquired pneumonia is different in recent studies compared with earlier studies. The following are possible reasons:

- An increasing proportion of ambulatory patients have some degree of decreased immune function that may be a factor.
- A number of new microorganisms causing pneumonia have been recently described, and methods for identifying these agents have become available in the clinical laboratory.
- Frequent administration of antibiotics early in the course of disease, and before diagnostic studies are obtained, may contribute to a higher proportion of cases of pneumonia that have no identifiable pathogen.

These factors may explain why many types of microorganisms have been implicated in pneumonia and why in a great number of cases an etiologic agent is not identified. In one study of community-acquired pneumonia in adults, about 70% of whom had an underlying medical condition, a definitive or presumptive cause was

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ABBREVIATIONS USED IN TEXT
HIV = human immunodeficiency virus
MIC = minimum inhibitory concentration

found in only 67%.[1] The two most common pathogens identified were *S pneumoniae* (pneumococcus, 15.3%) and *Hemophilus influenzae* (10.9%). Fewer but about an equal number of cases were identified as being caused by *Legionella* species, *C pneumoniae*, and aerobic gram-negative bacilli. *Mycoplasma pneumoniae* was uncommon in this study group, as were viruses, staphylococci, and others. This study group, although representative of adult patients, may have had a high proportion of patients with chronic obstructive pulmonary disease, alcohol abuse, a malignant neoplasm, diabetes mellitus, or other chronic conditions that may alter the types of organisms associated with pneumonia. For example, preexisting disease was seen in as many as 75% of those in whom pneumococcal pneumonia developed as opposed to a much lower frequency of preceding disease in patients with *M pneumoniae*. Furthermore, about a third of the study group was immunocompromised from infection with the human immunodeficiency virus (HIV) or from other causes.

Another series included 154 episodes of community-acquired pneumonia in veterans, of whom only 79 had an etiologic diagnosis.[4] Of these, 13 had *L pneumophila* or *Legionella micdadei*, 12 had gram-negative enteric bacilli, and 8 had *S pneumoniae*. Among others, a diagnosis of pneumonia from *C pneumoniae* was made in 8 patients, and *M pneumoniae* was thought to be the etiologic agent in 3 patients. In another series with fewer patients having underlying diseases, the three agents (other than viruses and tuberculosis) that most often caused nonpneumococcal community-acquired pneumonia were *M pneumoniae*, *Legionella* species, and *C pneumoniae*.[6]

An identified nonviral organism associated with pneumonia and considered to have features different from lobar pneumococcal pneumonia—that is, atypical pneumonia—was *M pneumoniae*, identified and isolated in the 1960s. These organisms are free-living bacteria that lack a cell wall but that can be grown using appropriate culture media. *Mycoplasma pneumoniae* is responsible for 15% to 35% of cases of pneumonia in outpatients, occurring in patients with and without underlying disease. Although usually associated with a healthy younger group of patients who are often confined in close quarters such as a family unit, military base, or dormitory, pneumonia from *M pneumoniae* is an important disease in older persons in whom severe pneumonia requiring a hospital stay may be seen.[7,8]

The epidemic of legionnaires' disease seen in Philadelphia, Pennsylvania, in 1976 triggered an intense effort that resulted in the identification of the responsible pathogen, *Legionella pneumophila*. These aerobic gram-negative bacilli were subsequently found to have been a causative agent in a number of previously undiagnosed cases of pneumonia. Since then, some 20 other *Legionella* species have been associated with pneumonia. These organisms are responsible for both episodic and epidemic outbreaks in the community and in hospitalized patients. Outbreaks have often been associated with contamination of the hot water supply; person-to-person spread does not occur. Among cases of community-acquired pneumonia, *Legionella* species is the causative organism in 1% to 15%, and patients frequently are older and have a history of cigarette smoking.[9,10]

Chlamydia pneumoniae was identified only within the past decade, and the name "TWAR," taken from identification labels of initial laboratory isolates, is still occasionally used.[11,12] *Chlamydia trachomatis* and *Chlamydia psittaci* are the other known species of this genus, which are obligate intracellular organisms that can be seen by using electron microscopy. These organisms use the cellular apparatus of infected cells for energy production and replication. *Chlamydia pneumoniae* is responsible for about 6% to 12% of cases of adult community-acquired pneumonia, sometimes occurring sporadically and sometimes in epidemics.[1,6] Outbreaks among military personnel and college students support the notion that close contact with infected persons is a risk factor. Infection with *C pneumoniae* may be cyclical, with four-year cycles of increased infection rates having been demonstrated from serologic testing.

Gram-negative aerobic bacilli and staphylococci are other bacterial pathogens that cause pneumonia more frequently in certain patient groups. These organisms are infrequent colonizers of the upper respiratory tract in healthy persons, but increase in number in those requiring increasing supportive and medical care. Thus, although in-hospital patients frequently have gram-negative rods found in the oropharynx, as many as 42% of ambulatory patients in a health care facility also may be colonized by these organisms.[13] Pneumonia in nursing home patients, although acquired in the "community," is more often due to these bacteria than may be suspected.

Hemophilus influenzae pneumonia is seen with increased frequency in patients with chronic obstructive pulmonary disease, alcoholism, smoking, and HIV infection. In particular, *H influenzae* type b is most often associated with pneumonia. Although other serotypes and nontypable *Hemophilus* species are more often colonizers or involved with upper respiratory tract infections, these may also cause lower respiratory tract infection. In patients with chronic lung disease and recently in immunocompromised patients, *Moraxella (Branhamella) catarrhalis* has been reported as a cause of pneumonia.

Viruses remain important and are probably underidentified etiologic agents in community-acquired pneumonia. Although adenovirus may infect young adults, especially military recruits, pneumonia due to this agent is usually mild and self-limited. Varicella-zoster virus is associated with severe pneumonia in adults, but diagnosis is usually not a problem. Influenza virus is the most important cause of epidemic viral pneumonia, with

important implications for immunization in the most susceptible populations—older patients and those with long-term disease. Influenza can be mild or severe enough to result in death from respiratory failure; often bacterial superinfection is considered to be a factor. A diagnosis of influenza is usually made in conjunction with a known community spread of influenza virus. Consideration is particularly important because of the possible beneficial response from amantadine hydrochloride if given very early for influenza type A. Cytomegalovirus is an important pathogen in immunocompromised patients, especially those receiving immunosuppression following solid organ and bone marrow transplantation.

Mycobacterium tuberculosis must at least be considered in all patients with community-acquired pneumonia. Although risk factors and clinical presentation are important in assessing the likelihood of mycobacterial infection, tuberculosis in persons heretofore considered "low risk" is reported with increasing frequency. Therefore, any clinical suspicion of tuberculosis should be pursued. In appropriate geographical areas, fungal pneumonia caused by *Coccidioides* and *Histoplasma* organisms are important causes of community-acquired pneumonia.

Tuberculosis, fungal pneumonia—especially endemic mycoses such as *Coccidioides* and *Histoplasma* species, and *Aspergillus* and *Cryptococcus* organisms—and *Pneumocystis carinii* should be considered possible etiologic agents of pneumonia in HIV-infected patients. Although these pathogens are considered highly likely and, therefore, are appropriately sought in those with known HIV infection, patients with undiagnosed HIV may present with infection with one of these organisms.

Community-Acquired Pneumonia—Typical Versus Atypical

In view of the many possible pathogenic organisms responsible for community-acquired pneumonias, it would be important to identify and initiate therapy for the most likely etiologic agents. This concept has long been responsible for dividing community-acquired pneumonias into typical and atypical presentations.

Clinical features of typical pneumonia are often equated with the common clinical presentation of pneumonia caused by *Streptococcus pneumoniae* (pneumococcus). This presentation is characterized by the onset of productive cough with purulent green, yellow, or rust-colored sputum, fever, chills, pleuritic chest pain, leukocytosis, and lobar consolidation on chest radiograph. Patients often have underlying medical problems. Hypotension, mental status changes, lethargy, confusion, and disorientation may be other manifestations. Pneumococcal pneumonia is associated with severe disease and is a leading cause of death in older persons and those with immune systems that are inadequate.

Atypical pneumonia usually consists of the gradual onset of an irritating, nonproductive cough, occasional scanty sputum, myalgias and arthralgias, upper respiratory tract symptoms, and a lack of consolidation on chest radiographs. Patients less often have underlying medical conditions, mental status changes, or hypotension. In the past, atypical pneumonias usually have been associated with *Mycoplasma* species, but more recently *C pneumoniae* and other causes have been found. Although there may be distinguishing features such as hyponatremia, diarrhea, abnormal liver function test results, and high fever in pneumonia caused by *L pneumophila*, these patients are also considered to have features of atypical pneumonia. Atypical pneumonias have generally been regarded as having a milder course and a better outcome.

Studies have shown, however, that the clinical and radiographic features of pneumonia caused by organisms associated with atypical pneumonia are indistinguishable from pneumonia caused by *S pneumoniae* (typical pneumonia). In a study of 359 patients with community-acquired pneumonias, a comparison was done of 55 patients with *S pneumoniae*, 39 with *H influenzae*, 24 with *L pneumophila*, and 22 with *C pneumoniae*, and no significant differences were found between the clinical features or underlying conditions.[1] For example, sputum production occurred in 74% of those with pneumococcus but in 75% of those with *L pneumophila* and 62% of those with *C pneumoniae* as causes of pneumonia. Such features as a "viral-like" prodrome, chills, consolidation, and changes in mental status did not distinguish patients with these disorders. This study was limited in that only five patients were found to have *M pneumoniae*, and they were not included in this comparison. The investigators concluded that pneumonias due to *Chlamydia* and *Legionella* species did not show sufficient atypical features to distinguish them from pneumococcal or *H pneumoniae* pneumonia.

Several studies have not supported the concept that pneumonias caused by the organisms associated with atypical pneumonia are less severe. For example, in one study it was found that the patients with severe community-acquired pneumonia—defined as those requiring admission to hospital for respiratory failure, altered mental status, hypotension, multilobar disease, or pleural effusions—included 7 patients with *L pneumophila* among a total of 67 patients, compared with 11 with pneumococcus.[5] In another report, 64 patients with *M pneumoniae* required admission to a hospital.[7] Clinical features of these patients' illness were indistinguishable from those of other causes of pneumonia. Although none of the patients with *Mycoplasma* pneumonia died, this group made up 5% of the patients with pneumonia who required hospitalization.

Evaluating Cases of Community-Acquired Pneumonia

The evaluation of a case of suspected community-acquired pneumonia is directed at establishing a diagnosis of pneumonia, identifying the etiologic agent, and determining whether or not the patient needs to be admitted to a hospital.

Diagnosing community-acquired pneumonia from the history and the results of a physical examination is

usually not difficult, although some patients will have predominant features of upper respiratory tract symptoms and nonspecific findings on a chest examination. Symptoms suggestive of lower respiratory tract involvement include dyspnea and chest pain, but sputum production may be evidence of bronchitis rather than pneumonia. Although, as emphasized previously, pneumonia due to nonpneumococcal organisms cannot always be distinguished from typical pneumonia, the findings of relative bradycardia with high fever, altered mental status, diarrhea, hypophosphatemia, and renal insufficiency (*L pneumophila*); pharyngitis, bullous myringitis, arthritis, and skin rashes, including erythema multiforme (*M pneumoniae*); or pharyngitis, conjunctivitis, sinusitis, lymphadenopathy, and poor clinical response to erythromycin (*C pneumoniae*) may be helpful. Chills can occur in patients with pneumococcal pneumonia (58%), pneumonia from *L pneumophila* (42%), and pneumonia due to *C pneumoniae* (53%).[1]

A chest radiograph is helpful in confirming the presence of community-acquired pneumonia but may not be needed in every patient. Those at high risk or with immunocompromise, hypoxemia, severe symptoms, serious underlying disease, chronic lung disease, heart failure, or other high risks such as advanced age, as well as all patients in whom hospital admission is considered, should have a radiologic examination initially. In young healthy patients who will be treated as outpatients, a chest radiograph should be taken if there is poor initial response to treatment, a suspicion of immunocompromise, severe symptoms, or other unusual features of disease. The chest radiograph may occasionally be helpful in distinguishing pneumonia caused by *S pneumoniae* from other community-acquired organisms. For example, only small pleural effusions are usually seen with *M pneumoniae*, *L pneumophila*, and *C pneumoniae*; consolidation is unusual with *M pneumoniae* and *C pneumoniae*; and cavitation is rarely if ever a feature of pneumonia caused by the atypical agents, but may be seen with *L pneumophila*. Chest radiographs should be repeated in patients admitted to a hospital to follow the rate of resolution. Radiographs should be correlated with clinical features including fever, arterial blood gas determinations, and other findings. A second chest radiograph to document resolving pneumonia should be done in those patients who have an increased risk for lung cancer—smokers, those older than 40 years, and those with other risk factors—but complete clearance of the infiltrate may take longer than two months in some patients. In those with slow or poor radiographic resolution, further investigation may be indicated for the presence of chronic lung disease or malignancy.

Recently a mortality of 21% (14 patients) was found in a prospective study of 67 patients with severe community-acquired pneumonia, defined as those having respiratory failure, septic shock, extrapulmonary septic complications, altered mental status, multilobar involvement, or cavitation.[5] Of 32 patients with an etiologic diagnosis, 12 (38%) had *S pneumoniae*, 7 (22%) had *L pneumophila*, and 8 (25%) had gram-negative bacilli. Risks for death included advanced age, the presence of other severe disease, and septic shock.

Sputum examination and culture are often insensitive and nonspecific in determining the etiologic agent; therefore, these tests should be done selectively in patients with community-acquired pneumonia. In a recent consensus statement of the American Thoracic Society, the value of the Gram's stain of sputum was questioned because of the lack of studies comparing sputum Gram's stain results and cultures of alveolar material.[3] Although for a healthy young patient, empiric treatment usually is given based solely on a clinical estimate of the most likely cause, a Gram's stain of sputum—but not culture because of its poor sensitivity and specificity—can be helpful in suggesting but not confirming the presence of *S pneumoniae*. In those with chronic lung disease, Gram's stain findings may suggest *H influenzae*. On the other hand, the absence of organisms on Gram's stain supports but does not confirm pneumonia due to *L pneumophila*, *M pneumoniae*, *C pneumoniae*, or virus.

If *L pneumophila* is suspected, direct immunofluorescence of sputum is occasionally positive, but this test is relatively insensitive. The presence of *L pneumophila* antigen in the urine can provide rapid evidence of acute infection, whereas a rise in antibody titer to *L pneumophila* is helpful only for making a retrospective diagnosis. Although serum cold agglutinins may be present in patients with *M pneumoniae* (presumptive diagnosis if present in a titer of 1:64 or higher), these are insensitive and nonspecific; a fourfold rise in complement fixation antibody titer measured during and after the resolution of disease can provide retrospective confirmation of infection. A diagnosis of pneumonia due to *C pneumoniae* can be made from serologic evidence of a rise in immunoglobulin M or G levels against *Chlamydia* species between the acute and convalescent periods.

Blood cultures should be done in all patients admitted to a hospital with pneumonia. In selected patients, especially those with decreased immunity, additional studies may be warranted, including acid-fast stains of sputum and other specimens, mycobacterial and fungal cultures, viral cultures and serologic tests, fiberoptic bronchoscopy, and lung biopsy. Transtracheal aspiration, the insertion of bronchoscopic protected-brush catheters, bronchoalveolar lavage, or needle aspiration of the lung should not be done unless there is a need for a rapid specific diagnosis or a particular indication is present.

The agent causing community-acquired pneumonia may not be confined to the lungs. Infection can extend to the pleural space, resulting in empyema that may require tube or surgical drainage for appropriate resolution. Bacteremia may spread to the meninges—*S pneumoniae*, *H influenzae*, gram-negative bacilli—heart, joints, pericardium, and other locations in both immunocompetent and immunodeficient patients.

Treatment

Fewer than 10% of young healthy patients with pneumonia will be ill enough to require admission to a hospital. The other 90% can be treated successfully as outpatients. Older patients and those with underlying diseases will require hospital care in as many as 80% of cases, however. Considerations for admission to the hospital may include the following[1,3,5,7,14]:

- The need for careful monitoring for the development of signs of respiratory failure or sepsis—underlying lung disease, chronic obstructive lung disease, hypoxemia, multilobar involvement, hypotension, or extreme leukocytosis or leukopenia;
- The need for parenteral antibiotics—respiratory failure, sepsis, pneumonia complicated by abscess or empyema, or an inability to take oral medications;
- Extrapulmonary complications such as meningitis;
- Severe underlying disease or compromise of the immune system—diabetes mellitus, liver disease, heart failure, renal failure, HIV infection, cancer, or corticosteroid use; or a previous need for admission to hospital for community-acquired pneumonia; and
- The presence of predictors of increased mortality or a complicated course—tachypnea, hypotension, the need for vasopressors, extrapulmonary infection, altered mental status, abnormal renal function, cavitation, pleural effusion, anemia, disseminated intravascular coagulation, or coagulopathy.

Patients with severe complications of pneumonia, such as hemodynamic compromise or respiratory failure, are best managed in an intensive care unit. A failure to respond to treatment in a reasonable time—48 to 72 hours as an outpatient—is also an indication for admission to hospital.

The choice of antibiotic for patients with community-acquired pneumonia is made using a combination of clinical suspicion, epidemiologic factors, underlying medical condition, and the results of Gram's staining. The lack of a proven ability to distinguish pneumococcal pneumonia from those organisms associated with atypical pneumonia, plus the recognition of the increased importance of *M pneumoniae*, *L pneumophila*, and *C pneumoniae* in both hospitalized and nonhospitalized patients with pneumonia has led to the choice of erythromycin as empiric therapy for many patients with community-acquired pneumonia. In the earlier-described study of 359 cases, for example, 71% of the etiologic agents identified would likely have been susceptible to erythromycin.[1] Erythromycin is effective against *S pneumoniae* and *L pneumophila* (when 1 gram is given 4 times a day) and is associated with a decreased duration of symptoms in pneumonia caused by *Mycoplasma* and *Chlamydia* organisms. In patients in whom *C pneumoniae* as the cause of pneumonia is strongly suspected, treatment with tetracycline or doxycycline may be preferred over the use of erythromycin, but these antibiotics are less effective against pneumococci and *Legionella* species. Rifampin can be used in conjunction with erythromycin for *L pneumophila*. Clinical experience with the newer macrolide antibiotics, clarithromycin and azithromycin, for the treatment of pneumonia caused by *C pneumoniae*, *M pneumoniae*, and *L pneumophila* is limited.

Although often chosen for the empiric treatment of pneumonia, cephalosporins given alone are not usually the treatment of choice in pneumonia without an identified cause. Second-generation cephalosporins such as cefuroxime are effective against *S pneumoniae*, *H influenzae*, and *M catarrhalis*, but they are not useful in treating *Mycoplasma*, *Chlamydia*, and *Legionella* species. Cephalosporins should generally be reserved for patients with chronic obstructive lung disease, alcoholism, or other conditions that predispose to pneumonia caused by organisms susceptible to these agents. The combination of erythromycin plus a second-generation cephalosporin may be indicated in patients with pneumonia for whom broader antibacterial coverage is needed because of advanced age or underlying comorbid conditions. Of note, the prospective study of 67 patients described earlier found that mortality was 15% (7 of 47 patients) in those with severe community-acquired pneumonia when the initial antibiotic regimen included erythromycin plus tobramycin or cefamandole (second-generation cephalosporin), but of 19 patients who were given other regimens, 6 (32%) died.[5]

A 1993 ad hoc committee of the American Thoracic Society addressed initial empiric antibiotic therapy for community-acquired pneumonia and made similar recommendations.[3] They recommended that outpatients younger than 60 years without other medical problems—including the risk of HIV—be given erythromycin or tetracycline as initial empiric treatment. For these patients, the likelihood that the pneumonia was caused by an organism susceptible to these antibiotics was considered high. For outpatients older than 60 years or who have other medical conditions, it was recommended they be given a second-generation cephalosporin or the combination of trimethoprim and sulfamethoxazole or a β-lactam antibiotic plus β-lactamase inhibitor such as the combinations of ampicillin sodium and sulbactam sodium or amoxicillin and clavulanate potassium, and each of these regimens should have erythromycin added if there is a sufficient suspicion of *L pneumophila*. The recommendations for those with pneumonia severe enough to be admitted to a hospital reflect a greater concern for gram-negative organisms, as second- or third-generation cephalosporins or a β-lactam–β-lactamase inhibitor is recommended with or without erythromycin. In patients admitted to a hospital with community-acquired pneumonia in whom broad empiric coverage is essential, the American Thoracic Society committee recommended both a macrolide (erythromycin) and a third-generation cephalosporin with activity against gram-negative bacilli, especially one with anti-*Pseudomonas* activity, such as ceftazidime.

The duration of treatment with antibiotics depends

on a patient's clinical response; specific recommendations cannot be made. Intravenous antibiotics should be given to patients admitted to hospital with serious disease, especially those with bacteremia, extrapulmonary manifestations, sepsis, respiratory failure, or immunocompromised conditions. If there is an adequate clinical response, including decreased fever and leukocytosis, improvement in the chest radiograph, and resolution of the factors defining severe pneumonia, the regimen can be switched to an appropriate oral antibiotic after three to six days to complete a two- to three-week course. In those treated on an outpatient basis who do not have features of pneumonia that necessitate hospitalization, oral antibiotics can be given for the entire treatment course with careful follow-up to ensure that symptoms resolve appropriately. The total duration of treatment should be tailored to a patient's clinical condition, especially the presence of underlying long-term illness and the capacity of the immune system.

If and when a specific pathogen is identified and the clinical course is consistent with this finding, directed therapy can then be given. Patients with proven *S pneumoniae* pneumonia are almost always treated effectively with intravenous penicillin G or, if clinical manifestations are less severe, oral penicillin V. Despite isolated reports, antibiotic-resistant *S pneumoniae* has been considered rare in the United States. For example, in data reported to the Centers for Disease Control from 1979 to 1987, about 5% to 10% of *S pneumoniae* isolates were resistant to penicillin (minimum inhibitory concentration [MIC] $\geq$ 0.1 μg per ml) and only 0.3% were resistant to erythromycin,[15] although rates of antibiotic resistance were reported higher in some regions of the country, such as Alaska and the southwestern states. On the other hand, isolates in parts of Europe and in South Africa are frequently resistant to penicillin and other antibiotics, with as many as 50% to 70% of isolates showing relative or high penicillin resistance. Much of the attention to antibiotic-resistant *S pneumoniae* has been focused on meningitis because of the need to achieve antibiotic levels in the cerebrospinal fluid that exceed the increased MIC of the resistant organisms.[16] The importance of antibiotic-resistant *S pneumoniae* in adults with pneumonia remains uncertain. A study in Spain of adults with bacteremic penicillin-resistant *S pneumoniae* pneumonia found an increased association with the presence of underlying diseases (malignancy, liver disease, alcoholism), recent antibiotic use (65% within 3 months), recent hospitalization, an episode of pneumonia within the past year, and greater clinical severity compared with patients with nonpenicillin-resistant *S pneumoniae* infection.[17] Mortality was also significantly higher. In patients with intermediate resistance to penicillin (MIC 0.12 to 2.0 μg per ml), treatment with high-dose penicillin appeared to be successful, but those with more highly resistant organisms responded poorly. The ideal treatment of adults with pneumonia caused by known or suspected antibiotic-resistant *S pneumoniae* has not yet been defined.[16] One approach to *S pneumoniae* pneumonia in the United States would be to look for antibiotic-resistant organisms if there is a high community or hospital prevalence of resistance, if the patient has received antibiotics within the past three months, if pneumonia is clinically severe, or if meningitis is suspected. In these patients, therapy with either higher doses of penicillin (2 to 4 million units every 4 to 6 hours) or vancomycin hydrochloride can be started until susceptibility results become available.[16]

Some strains of *H influenzae* produce β-lactamase, so that second- and third-generation cephalosporins or drugs such as amoxicillin-clavulanate should be given when pneumonia is caused or suspected to be caused by these organisms. β-Lactamase production is commonly found with *M catarrhalis* infection; treatment generally is with amoxicillin-clavulanate, trimethoprim-sulfamethoxazole, or third-generation cephalosporins.

Prevention

Physicians have long been aware of the continued high mortality or severe complications from *S pneumoniae* pneumonia in certain subgroups of patients despite prompt and correct antibiotic therapy. Pneumococcal vaccine, intended to immunize against 23 serotypes of *S pneumoniae*, has been shown to be effective in 50% to 60% of patients in preventing pneumonias caused by these organisms. Moreover, these 23 serotypes include approximately 80% to 85% of the *S pneumoniae* causing severe pneumonia with bacteremia or central nervous system involvement.

Pneumococcal vaccination is currently recommended for all patients older than 65 years and for selected subgroups. These subgroups include patients with some degree of immunosuppression, such as those with functional asplenism, splenectomy, organ transplants, nephrotic syndrome, renal failure, diabetes mellitus, or those receiving cancer chemotherapy. Others who should receive vaccination are patients with chronic congestive heart failure, chronic lung disease, alcoholism, and cirrhosis.

Immunization against other organisms that cause pneumonia is not available. Because pneumonia frequently complicates influenza in older patients and in patients with chronic illness, however, yearly influenza vaccination is also recommended for the prevention of pneumonia.

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